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| 10/681,752 | 10/09/2003 | Dongan Wang | 116567-022 | 8132 |

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K&L Gates LLP
P.O. BOX 1135
CHICAGO, IL 60690

| EXAMINER | |
|---|---|
| SCHUBERG, LAURA J | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/681,752 | WANG ET AL. | |
| | Examiner | Art Unit | |
| | Laura Schuberg | 1657 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *40,42,43,46-49,60 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40,42,43,46-49,60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/15/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

This action is responsive to papers filed 04/23/2009.

Claim 40 has been amended. No claims have been newly added or newly canceled.

Currently claims 40, 42, 43, 46-49, 60 and 61 are pending and have been examined on the merits.

***Previous Rejections***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 40, 42, 43, 46-49, 60 and 61 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney et al (US 5,900,245) in view of Hai et al (Bioconjugate Chem. 2000).**

Amended claim 40 is drawn to a method of integrating a hydrogel to a musculoskeletal tissue, comprising: a) priming the surface of a musculoskeletal tissue by treating with the musculoskeletal tissue with a priming agent to create a primed musculoskeletal tissue, wherein the priming agent comprises a polysaccharide with at

least one aldehyde group and a first at least one free radical polymerizable group, and the aldehyde group reacts with the musculoskeletal tissue to covalently bind the tissue and the priming agent; b) adding to the primed tissue a polymerizable agent and a radical photoinitiator, wherein the polymerizable agent comprises a biocompatible polymer having a second at least one free radical polymerizable group; and c) reacting the primed musculoskeletal tissue and the polymerizable agent by a radical reaction to create an integrated hydrogel covalently bound to the musculoskeletal tissue.

Claim 42 includes wherein the musculoskeletal tissue is disposed in a mammal.

Claim 43 is drawn to the method of claim 40 further includes wherein the polysaccharide is chondroitin sulfate.

Claim 46 are drawn to the method and hydrogel of claim 40 and further includes wherein the reacting step further comprises exposing the primed tissue and the polymerizable agent to a source of electromagnetic radiation.

Claims 47-49 include wherein the polymerizable agent comprises biologically active material, autologous cells, or growth factor.

Claim 60 is drawn to the method of claim 46 and includes wherein the musculoskeletal tissue is a bone or cartilage.

Claim 61 is drawn to the method of claim 46 and includes wherein the radiation is ultraviolet.

Sawhney teaches a method of adhering preformed barriers or coatings to tissue by first priming the surface of the tissue, adding a polymerizing agent to the primed surface and allowing polymerization to take place (column 3 lines 17-26). Cartilage and

bone are specifically taught to be suitable tissues for use in the method (column 12 line 28). Ultraviolet radiation is taught as being used to form covalent bonds with crosslinkable groups of the polymerizable agent to form a hydrogel (column 8 lines 28-55). The preferred crosslinkable groups include acrylate, a diacrylate, oligodiacrylate, methacrylate, dimethacrylate, and oligomethacrylate and aldehydes (column 8 lines 40-48). The addition of diffusible drug substances, growth factors (column 12 line 35-column 13 line 59) and living cells (column 14 lines 15-17) to the polymerizable agent is taught as well. Autologous cells are suggested as well (column 26 lines 8-25). Wherein a monomer is added with an initiator in a first step and then a monomer is added in a second step to activated tissue, resulting in polymerization on the tissue is also taught (column 6 lines 15-26). Monomers with at least two polymerizable groups (such as acrylate groups) are suggested as well (column 7 lines 54-65).

Sawhney et al do not specifically include wherein the primer is a polysaccharide, such as chondroitin sulfate, with an aldehyde group.

Hai et al teach the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai et al teach that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the *in vivo* properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai et al would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice with regard to Sawhney et al based on the fact that Hai et al teach the use of

chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because Sawhney et al suggest the use of the claimed crosslinkable groups and polysaccharides such as chondroitin sulfate for the method as well (column 8 line 27-column 9 line 26). The carrying out of the obvious method steps would then produce the integrated hydrogel as claimed.

Therefore, the combined teachings of Sawhney et al and Hai et al render obvious Applicant's invention as claimed.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 40, 42, 43, 46-49, 60 and 61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-75 of copending Application No. 11/369,578.** Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application anticipate the claims of the current application since musculoskeletal tissue includes bone and osteochondral tissue.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 40, 42, 46-48, 60 and 61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 10, 15 of copending Application No. 10/962,278 in view of Hai et al (Bioconjugate Chem. 2000).**

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

**Claims 40, 42, 46-48, 60 and 61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-7, 15, 18, 22 of copending Application No. 11/637,516 in view of Hai et al (Bioconjugate Chem. 2000).**

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

**Claims 40, 42, 46, 47, 49, 60 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53, 63, 65, 77 of copending Application No. 10/681,753 in view of Hai et al (Bioconjugate Chem. 2000).**

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

***Response to Arguments***

Applicant's arguments filed 04/23/2009 have been fully considered but they are not persuasive.

Applicant argues that the Sawnhey primer is not bi-functional as the present priming agent is.

This is not found persuasive because while Sawhney does not specifically teach a polysaccharide with an acrylate and an aldehyde group as the primer, Sawhney does suggest that a monomer can be included in the priming step (column 6 lines 15-25) and that this monomer can have two polymerizable groups (column 7 lines 54-65) which would make it bi-functional.

Applicant argues that Sawhney does not crosslink the second surface or preformed barrier/coating to form an integrated hydrogel. Applicant asserts that in

Sawhney the second surface or preformed barrier/coating does not crosslink at all during polymerization of the layer of the polymerizable monomer.

This is not found persuasive as Sawhney does teach the polymerization of the primer layer with the polymerizable layer on the tissue surface (column 6 lines 15-25).

Applicant argues that the Sawhney method is suitable only for the type of surface which can be stained by the priming initiator, while the present method does not have such a limitation.

This is not found persuasive because the Sawhney reference includes many embodiments some of which render the claimed invention obvious. As long as the Sawhney reference includes some embodiments that are suitable for the claimed surface type, the reference method can be used to demonstrate obviousness of the claimed invention.

Applicant argues that the Hai reference does not disclose the use of chondroitin sulfate with a tissue surface and therefore does not disclose or contemplate modification of a tissue surface.

This is not found persuasive because Hai specifically suggests using chondroitin sulfate *in vivo* for its therapeutic utility and that changes in the surface charge or charge density of the red cell membrane are induced by the adherent macromolecule (page 712, column 2). Clearly its affect on proteins would suggest its affects on the proteins present in the cell membranes of tissue surfaces as well. Since Sawhney suggest the use of monomers that have two polymerizable groups and that these polymerizable groups can be acrylates and/or aldehydes, the teaching of the therapeutic benefits of

chondroitin sulfate with an aldehyde group by Hai et al make it an obvious choice for inclusion in the method of Sawhney as a suitable monomer and for modification with additional groups (such as acrylates) as suggested by Sawhney as well.

Applicant argues that the Sawhney method is not suitable for cartilage surfaces and that Sawhney therefore teaches away from the presently claimed invention.

This is not found persuasive because Sawhney specifically suggests cartilage as well as bone as suitable surfaces for treatment (column 12 line 28).

Therefore the claims remain rejected as obvious over the prior art as cited above.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg